

**S2 Text.** Nondimensional analysis and sensitivity analysis. In order to nondimensionalize the system for further analysis, consider the substitutions  $t = T\tau$ ,  $N(t) = \hat{N}n(\tau)$ ,  $N_d(t) = \hat{N}n_d(\tau)$ ,  $A(t) = \hat{A}a(\tau)$ ,  $P_0(t) = \hat{P}_0p_0(\tau)$ , and  $B(t) = \hat{B}b(\tau)$  where  $\tau$ ,  $n$ ,  $n_d$ ,  $a$ , and  $p_0$  are dimensionless.

When substituting the above equations, eqs. (19) to (22) reduce to the following system:

$$\frac{dn}{d\tau} = - \left( \frac{\lambda_d \hat{A} a}{\hat{A} a + \alpha_0} \right) T n + \left( \lambda_d - \frac{\lambda_d \hat{A} a}{\hat{A} a + \alpha_0} \right) T n_d, \quad (1)$$

$$\frac{dn_d}{d\tau} = \left( \frac{\lambda_d \hat{A} a}{\hat{A} a + \alpha_0} \right) T n - \left( \lambda_d - \frac{\lambda_d \hat{A} a}{\hat{A} a + \alpha_0} \right) T n_d - \mu_d T n_d, \quad (2)$$

$$\frac{da}{d\tau} = \left( \frac{k_A \hat{N}^2 T}{\hat{A}} \right) (n_d^2 + n_d n) - k_{P_0} T \hat{P}_0 a p_0, \quad (3)$$

$$\frac{dp_0}{d\tau} = \left( \frac{k_R \rho_R \hat{B} b_T}{\hat{P}_0} \right) \hat{N} T n - k_{P_0} T \hat{A} a p_0. \quad (4)$$

If  $T = \lambda_d^{-1}$ ,  $\hat{N} = \sqrt{\lambda_d \alpha_0 k_A^{-1}}$ ,  $\hat{A} = \alpha_0$ ,  $\hat{P}_0 = \lambda_d (k_{P_0})^{-1}$ , and  $\hat{B} = \lambda_d \hat{P}_0 (k_B \hat{N})^{-1}$  then eqs. (1) to (4) simplify to

$$\frac{dn}{d\tau} = - \frac{an}{a+1} + \left( 1 - \frac{a}{a+1} \right) n_d, \quad (5)$$

$$\frac{dn_d}{d\tau} = \frac{an}{a+1} - \left( 1 - \frac{a}{a+1} \right) n_d - c_0 n_d, \quad (6)$$

$$\frac{da}{d\tau} = n_d^2 + n_d n - ap_0, \quad (7)$$

$$\frac{dp_0}{d\tau} = b_T n - c_1 a p_0, \quad (8)$$

where  $c_0 = \mu_d (\lambda_d)^{-1}$ , and  $c_1 = k_{P_0} \alpha_0 (\lambda_d)^{-1}$ .

With this nondimensionalization, the model is now reduced to a system of three parameters: the timescale,  $T$ , and  $c_0$  and  $c_1$ . The system can now be studied in a simplified form.

**S1 Table.** Index of values of nondimensionalized system parameters and scaling factors

Variable	Definition	Value
$c_0$	$\mu_{n_d} \lambda_d^{-1}$	$8.2 \cdot 10^{-2}$
$c_1$	$k_{P_0} \alpha_d \lambda_d^{-1}$	12.2623
$T$	$\lambda_d^{-1}$	16.3934 days
$\hat{N}$	$\sqrt{\lambda_d \alpha_0 k_A^{-1}}$	4.1231 vol. <sup>-1</sup>
$\hat{A}$	$\alpha_0$	17 day <sup>-1</sup>
$\hat{P}_0$	$\lambda_d k_{P_0}^{-1}$	1.3864 vol. <sup>-1</sup>
$\hat{B}$	$\lambda_d \hat{P}_0 (k_R \rho_R \hat{N})^{-1}$	$1.74 \cdot 10^{-2}$ mg · kg <sup>-1</sup>

With the nondimensionalized system given in eqs. (5) to (8), we can investigate the behavior of the system in neighborhoods about  $c_0$  and  $c_1$  over a 90 day period, thus  $T$  is fixed.

Before we investigate the sensitivity of the system to the parameters, we define the following differences:

$$\Delta N = N(t_f) - N(t_0) = \hat{N} (n(\tau_f) - n(\tau_0)), \quad (9)$$

$$\Delta N_d = N_d(t_f) - N_d(t_0) = \hat{N} (n_d(\tau_f) - n_d(\tau_0)), \quad (10)$$

$$\Delta A = A(t_f) - A(t_0) = \hat{A} (a(\tau_f) - a(\tau_0)), \quad (11)$$

$$\Delta P_0 = P_0(t_f) - P_0(t_0) = \hat{P}_0 (p_0(\tau_f) - p_0(\tau_0)), \quad (12)$$

where  $t_f=90$  days, and  $t_0=0$  days. Changes with respect to  $c_0$  and  $c_1$  will be computed in the nondimensional system and then scaled to be dimensionful. Note that both Fig 4 and Fig 5 are centered about our calculated values of  $c_0$  and  $c_1$  given in Table 1.

Without treatment, there is no ApoE is introduced to the system, and thus the system is invariant to changes in  $c_1$ . It can be seen in Fig 4 that changes in  $c_0$  do not significantly alter the behavior of the system.

With bexarotene added to the simulation, Fig 5 shows that  $c_0$  and  $c_1$  do not cause significant variation in  $\Delta N$ . Furthermore, while  $c_1$  has an influence on  $\Delta N_d$ , it is influenced more heavily by  $c_0$ . With the introduction of bexarotene, the behavior of  $\Delta A$  has changed and is now dominated by changes in  $c_0$ , as is  $\Delta P_0$ .